Non-Technical Abstract

Elimination of leukemia following allogeneic bone marrow or stem cell transplantation (hematopoietic cell transplantation; HCT) is in part attributable to a "graft-versus-leukemia" (GVL) reaction mediated by immune cells derived from the bone marrow/stem cell donor. Despite the potency of the GVL effect, however, relapse of acute leukemia following allogeneic HCT occurs in a significant fraction of patients, particularly those transplanted in an advanced stage of disease. Treatment of posttransplant relapse with infusions of unselected immune cells from the donor in an attempt to harness the GVL effect produces responses in a small number of patients, but these responses are transient and are accompanied by significant toxicity including graft-versus-host disease (GVHD). Because posttransplant relapse is ultimately fatal in the majority of patients in which it occurs, novel strategies for treating relapse are required. The proposed study will investigate the safety of a new type of therapy for posttransplant relapse that involves the administration of immune cells derived from the donor which can specifically recognize and kill blood cells, including leukemic cells, but not fibroblasts (a type of non-blood-derived cell) from the recipient. It is anticipated that the infusion of cells that are selective for blood cells derived from the recipient will produce a GVL effect without inducing GVHD. To further improve the safety of this form of therapy, the first 3 infusions will consist of cloned immune cells that have been transduced with a retrovirus containing a hygromycin phosphotransferase – *Herpes simplex* virus thymidine kinase fusion gene (termed HyTK). Cells expressing the bifunctional HyTK fusion gene are hygromycin resistant but are also sensitive to ganciclovir or acyclovir. Modification of the immune cells to express the HyTK gene will allow their elimination *in vivo* if the infusions are associated with GVHD or other toxicity.